**Food and Drug Administration**
**Center for Drug Evaluation and Research**
*Anti-Infective Drugs Advisory Committee*
December 9, 2009

Questions for the Committee

## Endpoints

1. Should all-cause mortality be the primary endpoint in noninferiority clinical trials that evaluate new antibacterial drugs for CABP? (Vote Yes/No)

   If Yes:

   a. Please explain your rationale.

   b. Please comment on the acceptable noninferiority margin and timepoint for assessment of all-cause mortality (i.e. a point in time after randomization in a clinical trial or a point in time after completion of clinical trial drug therapy).

   c. You may also wish to comment on items 1e. and 1f. below.

   If No:

   d. Please explain your rationale.

   e. Please comment on what other study designs should be used for assessment of all-cause mortality as an endpoint.

   f. Please comment on what other primary endpoints should be studied. Provide your rationale for the recommended primary endpoint; and if your proposal relies upon a noninferiority design, provide your justification for the proposed noninferiority margin.

2. Do the historical data presented support the use of clinical response as the primary endpoint at an earlier time point (e.g. 48-72 hours) in a noninferiority trial? (Vote Yes/No)

   If Yes:

   a. Please explain your rationale.

   b. Please discuss the appropriate study population for a noninferiority trial that relies upon clinical response (e.g., at 48-72 hours) as its primary endpoint. In your comments, you might consider:

      i. the characteristics of the population from which the historical information is derived.

ii. to what CABP populations (e.g., degree of CABP severity or mortality rate in the study population) the treatment effect for clinical response at 48-72 hours would apply; and whether there are CABP populations for which clinical response at 48-72 hours is not an appropriate endpoint.

c. If clinical response at 48-72 hours is the primary endpoint, are there any comments you wish to provide on how mortality should be analyzed considering that the study likely would not be powered to analyze mortality.

If No:

d. Please explain your rationale and any other comments.

**Assessing CABP Severity at time of Enrollment**

3. Should scoring systems such as PORT/CURB-65 be used to enroll patients or would it suffice to enrich the population based on age ≥50 years? (Non-voting question, please explain your rationale.)

***Legionella pneumophila***

4. Should patients with documented *L. pneumophila* be enrolled in noninferiority CABP trials? (Vote Yes/No)

If Yes:

a. Please explain your rationale.

b. Please describe the characteristics of patients (e.g., disease severity) with *L. pneumophila* appropriate for inclusion in a non-inferiority CABP trial.

c. What is the appropriate primary endpoint for a noninferiority trial which includes patients with *Legionella*?

If No:

d. Please explain your rationale.

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